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investor Update

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# PEGASYS doubles the efficacy in difficult-to-treat Hepatitis B virus versus conventional Interferon

Study results presented today at the 11th International Symposium on Viral Hepatitis and Liver Disease, Sydney Australia demonstrate that PEGASYS, a new generation hepatitis C therapy, more than doubled the efficacy of conventional interferon in the treatment of chronic hepatitis B (CHB).

PEGASYS given for six months at the same 180 mg dose as in hepatitis C, showed a combined end point of HBeAg loss, HBV DNA below 500,000 copies/ml and normalisation of ALT, of 28% compared to 12% for conventional interferon (Roferonâ A: 4.5 MIU).

The Phase II study assessed the efficacy of PEGASYS in patients with difficult-to-treat HBeAg-positive CHB, which was defined as high pre-treatment HBV DNA (high levels of replicating virus in the patient's liver) and low pre-treatment ALT (indicating a weak natural response from the patients immune system to HBV). These factors are considered predictors of a poor response to HBV therapy. As in hepatitis C, where genotype 1 is considered difficult to treat, there is also evidence that those infected by the HBV genotype C virus respond less well to treatment.

"Until now, there was only a slim chance that these hepatitis B patients could be cured of their disease," said Professor Graham Cooksley, the lead investigator of the study and Senior Principal Research Fellow, Clinical Research Centre, Royal Brisbane Hospital, Australia. "These monotherapy results are extremely positive and demonstrate the same kind of efficacy in hepatitis B as we saw with genotype 1 patients in hepatitis C. PEGASYS works very well in those with the most treatment-resistant disease."

PEGASYS fared better than conventional interferon in every efficacy parameter measured. The efficacy parameters were:

- · HBeAq loss (loss of viral protein indicates that viral replication has stopped)
- · HBV DNA below 500, 000 copies/ml (a level that indicates the virus is being effectively controlled)
- normalisation of ALT (normal ALT enzyme level reflects normal function of the liver) When all of the response criteria noted above are met, this is described as a "combined response."

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THOMSON FINANCIAL Results in difficult-to-treat HBV Disease

- In patients with low pre-treatment ALT (0-2 x upper limit of normal), the combined response was achieved in 27% of patients treated with PEGASYS compared to 11% of patients treated with conventional interferon.
- In patients with high pre-treatment HBV DNA ( > log 8.5 HBV DNA), the combined response was achieved in 20% of patients on Pegasys compared to 14% of patients treated with conventional interferon.
- In patients with HBV genotype C, the combined response was achieved by 21% of PEGASYS patients compared to 6% of interferon patients.

The 194 patients in the study were treated with either conventional interferon three times weekly or PEGASYS (at 90 mg, 180 mg or 270 mg) once weekly for a 24-week-period, and were then observed with no further treatment over the subsequent 24 weeks.

In addition to this research effort, there are two phase III studies approaching completion. These studies explore the benefit of a longer duration of treatment (48 weeks) where it is postulated that even higher response rates may be achieved based on data with conventional interferon. These studies, which use the same 180 mg dose, will also explore the efficacy of combining of PEGASYS with lamivudine, a nucleoside analogue.

## New Hope for HBV Sufferers

Currently, lamivudine, adefovir dipovoxil and conventional interferon alfa are the sole agents approved for the treatment of hepatitis B. However, these agents have clear limitations in terms of overall efficacy and about 20 per cent of patients treated with lamivudine develop resistance to the drug within one year of therapy. In addition, the majority of patients treated with lamivudine are required to continue therapy indefinitely. PEGASYS overcomes the limitations of current therapies; delivering higher efficacy within a defined treatment duration. Importantly, the hepatitis B virus is unlikely to develop resistance to PEGASYS.

#### About Hepatitis B

Hepatitis B is a blood-born virus that attacks the liver and is the most common serious liver infection in the world. The Hepatitis B virus is highly contagious and is relatively easy to transmit from one infected individual to another. It is 100 times more infectious than the HIV virus.

Despite a highly effective vaccine, More than two billion people have been infected by HBV and 350 million people have chronic infection, which can be easily transmitted by blood-to-blood contact, during birth, sex, and by sharing needles. For those chronically infected with HBV, treatment is the only option. Hepatitis B is the ninth leading cause of death in the world; left unchecked, it can cause liver cancer and death.

### About PEGASYS

PEGASYS, a new generation hepatitis C therapy that is different by design, provides significant benefit over conventional interferon therapy in patients infected with HCV of all genotypes. The benefits of PEGASYS are derived from its new generation large 40 kilodalton branched-chain polyethylene glycol (PEG) construction, which allows for constant viral suppression. PEGASYS also distributes more readily to the liver (the primary site of infection) than conventional interferon. PEGASYS is the only pegylated interferon available as a ready-to-administer solution. Each weekly subcutaneous injection contains 180mcg of pegylated interferon alfa-2a which is the recommended dose for all patients, regardless of body weight.

PEGASYS has been approved for the treatment of chronic hepatitis C in more than 70 countries, including the European Union and the United States. The most recent approvals for PEGASYS have occurred in China and New Zealand.

#### About Roche

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Headquartered in Basel, Switzerland, Roche is one of the world's leading research-oriented healthcare groups in the fields of pharmaceuticals and diagnostics. Roche's innovative products and services address prevention, diagnosis and treatment of diseases, thus enhancing people's well being and quality of life. In 2002 Roche's core businesses recorded sales of 26.5 billion Swiss francs and employed some 61,900 people worldwide.

Roche is committed to the viral hepatitis disease area, having introduced Roferon-A for hepatitis B and C, followed by PEGASYS in hepatitis C and now PEGASYS is demonstrating similar superior efficacy over conventional interferon in hepatitis B. Roche has also launched its own brand of ribavirin, Copegus, to be used in conjunction with Roferon A or PEGASYS for HCV. Roche also manufactures HBV and HCV diagnostic and monitoring systems: The COBAS AMPLICOR™ Test, and the AMPLICOR™ MONITOR Test, two testing systems used to detect the presence of, and quantity of, HBV DNA or HCV RNA in a person's blood. Roche's commitment to hepatitis has been further reinforced by the in-licensing of Levovirin, an alternative antiviral. Levovirin will be studied with the objective of demonstrating superior tolerability over the current standard, ribavirin.

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## Media Release



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Roche receives FDA clearance for Cobas Amplicor HIV-1 Monitor Test PCR-based test enhances ability to measure viral loads of HIV Patients

Roche today announced that it has received clearance from the U.S. Food and Drug Administration (FDA) for the Cobas Amplicor HIV-1 Monitor Test (version 1.5) an enhanced version of Roche's polymerase chain reaction (PCR) assay used to measure the amount of HIV-1 RNA (virol load) present in an infected person's blood,

The Cobas Amplicor HIV-1 Monitor Test (version 1.5) is an automated assay that amplifies and detects genetic material, allowing for accurate quantification of even small amounts of viral RNA in the blood. This new test can measure viral loads as low as 50 copies of HIV-1 RNA per millilitre (c/mL) of plasma. This level of sensitivity is critical for optimising treatment strategies, because maintaining an infected patient's viral load below 50 c/mL (undetectable) has been associated with a more complete and durable viral suppression. This assay is the automated version of the Amplicor HIV-1 Monitor Test (version 1.5) that received FDA approval last year.

The Cobas Amplicor HIV-1 Monitor Test (version 1.5) also has the enhanced ability to quantify HIV-1 Group M subtypes A-G. While HIV-1 subtype B continues to predominate in Western Countries, studies now confirm that the incidence of HIV-1 non-B subtypes is increasing all over the world. A test's ability to detect a broader range of these genetically diverse viruses will, therefore, be crucial to HIV patient care on a global basis.

"We are very pleased to receive FDA clearance for this newest generation of PCR HIV-1 viral load testing," said Heino von Prondzynski, Head of Roche Diagnostics and member of Roche's Corporate Executive Committee. "The Cobas Amplicor HIV-1 Monitor Test (version 1.5) will allow laboratories to deliver quality HIV viral load results in a shorter time, thanks to cutting edge automation."

According to the World Health Organization, more than 42 million people worldwide were living with HIV at the end of 2002, an infection rate that is expected to increase. The demand for antiretroviral therapy and consequently, viral load testing, is expected to rise accordingly. Roche Diagnostics provides both manual and automated HIV-1 RNA reagent kits and testing systems to laboratories throughout the world.

#### Roche in HIV

Roche is at the forefront of efforts to combat HIV infection and AIDS, committed since 1986 to groundbreaking research and development of innovative new drugs and diagnostic technology. Saquinavir was the first Protease Inhibitor (PI) and was first introduced by Roche in 1995 in the US. Fuzeon is the first fusion inhibitor, representing the first new class of anti-HIV treatments in seven years. Unlike all currently approved anti-HIV drugs, Fuzeon blocks the virus from entering the human immune cell.

## About Roche

Hendquartered in Basel, Switzerland, Roche is an innovation driven global healthcare leader focused on pharmaceuticals and diagnostics. Roche is worldwide number one in diagnostics and oncology and has a leading position in virology and transplantation. With products and services that address the prevention, diagnosis and treatment of diseases, the company contributes broadly to the enhancement of people's health and quality of life. Roche employs some 62,000 people in more than 150 countries around the world. The company has business alliances and R&D relationships with numerous partners, including majority ownership interests in Genentech and Chugai, which are both members of the Roche Group. Roche's Diagnostics Division, the world leader in in-vitro diagnostics with a uniquely broad product portfolio, supplies a wide array of innovative testing products and services to researchers, physicians, patients, hospitals and laboratories worldwide. For further information, please visit our websites www.roche.com.